

Attorney Docket No.: DRE-0067  
Inventors: Laurencin et al.  
Serial No.: 10/052,121  
Filing Date: January 17, 2002  
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#### REMARKS

Claims 1-6 are pending in the instant application. Claims 1-3, 5 and 6 have been rejected. Claim 4 has been withdrawn from consideration by the Examiner and subsequently canceled without prejudice by Applicants in this amendment. Claims 1, 3 and 6 have been amended. Support for these amendments is provided in the specification at page 1, lines 15-18, page 6, lines 17-20 and page 8, line 31 through page 9, line 4. Thus, no new matter is added by these amendments. Reconsideration is respectfully requested in light of these amendments and the following remarks.

#### I. Amendments to Specification

Amendments to the specification have been made to correct inadvertent typographical errors noted in reference citations disclosed in the specification during preparation of the Information Disclosure Statement. References listed and submitted with the Information Disclosure Statement and reviewed by the Examiner prior to preparation of the instant Office Action correspond to the reference citations corrected by this amendment. No new matter is added by these amendments and entry is respectfully requested.

#### II. Finality of Restriction Requirement

The Examiner has made final the Restriction Requirement mailed June 23, 2004. Thus, in an earnest effort to advance the prosecution of this case, Applicants have canceled non-elected claim 4 without prejudice. In light of the finality of this Restriction Requirement, Applicants reserve the right to file a divisional application to the canceled subject matter.

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**III. Rejection of Claims 1-3, 5 and 6 under 35 U.S.C. § 112, second paragraph**

Claims 1-3, 5 and 6 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In particular, the Examiner suggests that the recitation of "lighter than water or light as water microcarriers" is unclear because "light" is relative and subjective and can represent color. Thus, in accordance with the Examiner's suggestion and teachings in the specification at page 7, lines 1-3, Applicants have amended the claims to state that the microcarriers have a density equal to or less than the density of water.

Further with respect to claim 1, the Examiner suggests that the relationship of the microcarriers to the scaffold is also unclear. Accordingly, Applicants have amended claim 1 in accordance with teachings in the specification at page 1, lines 15-18, and page 8, line 31 through page 9, line 4 to clarify that the microcarriers are bonded together to form the scaffold.

With respect to claim 3 and 6, the Examiner suggests that the term "osteoblast-like" is uncertain as to meaning and scope because "like" is relative and subjective. Applicants respectfully disagree since experiments with exemplary "osteoblast-like" cells, namely MC3T3 cells, are described in detail in the specification. See page 10-11 of the specification.

However, in an earnest effort to advance the prosecution of this case, claims 3 and 6 have been amended to delete this term.

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Withdrawal of these rejections under 35 U.S.C. § 112, second paragraph, is therefore respectfully requested.

#### IV. Rejection of Claim 1 under 35 U.S.C. § 102(b)

Claim 1 has been rejected under 35 U.S.C. § 102(b) as being anticipated by Devin et al. The Examiner suggests that Devin et al. disclose degradable polymer-ceramic 3-dimensional composite matrices for use as a bone graft material. The Examiner suggests that the matrices obtained by Devin et al. are a scaffold as presently claimed and the microspheres inherently have a density less than or equal to the density of water.

Accordingly, in an earnest effort to advance the prosecution of this case, Applicants have amended claim 1 to clarify that the scaffolds of the present invention comprise biocompatible, biodegradable polymer-based hollow microcarriers with a density equal to or less than water bonded together into an interconnected, three dimensional scaffold. As taught at page 6, lines 17 through 20 and in further detail in Example 1 at page 14, to produce these scaffolds, polymer microencapsulation methods were adapted for formation of hollow, lighter than water or light as water microcarriers. It is with these hollow microcarriers that Applicants were able to produce scaffolds which circumvent limitations associated with static three-dimensional culturing methods such as taught by Devin et al., and increase the rate and extent of mineralized tissue formation in the rotating bioreactor as compared to prior art scaffolds.

Devin et al. does not teach hollow polymer-based microcarriers or methods adapted for their production.

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Accordingly, this reference cannot anticipate claim 1 as amended as it does not teach all the elements of the invention as now claimed. See MPEP § 2131.

Withdrawal of this rejection under 35 U.S.C. 102(b) is therefore respectfully requested.

**V. Rejection of Claims 1-3, 5 and 6 under 35 U.S.C. § 103(a)**

Claims 1-3, 5 and 6 have been rejected under 35 U.S.C. 103(a) as being unpatentable over Devin et al. in view of Spaulding (U.S. Patent 6,001,643) and Granet et al., and if necessary in further view of Kusano et al. (U.S. Patent 5,006,467), Henderson (U.S. Patent 4,448,884) or Starling (U.S. Patent 6,210,715). The Examiner suggests it would have been obvious to use the matrices of Devin et al. for cell culture in a roller bottle as disclosed by Spaulding or in a rotating-wall vessel as disclosed by Spaulding since these culturing techniques are intended for culturing cells on a carrier. The Examiner suggests that it would have been further obvious to provide the matrices with a density less than or equal to that of water as suggested by Spaulding so the matrices will surround the axis away from the wall. The Examiner suggests that, if needed, Kusano et al., Henderson or Starling et al. further suggest a density equal to that of water from disclosing cell culture with a microcarrier having a density of 1 g/ml or 1 g/cc. The Examiner suggests that culturing of osteoblast cells would have been obvious and if needed suggested by Granet et al. since these cells produce bone as desired by Devin et al.

Applicants respectfully traverse this rejection.

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To establish a *prima facie* case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art must teach or suggest all claim limitations.

As discussed in Section IV, *supra*, the primary reference Devin et al. does not teach or suggest a scaffold comprising hollow polymer-based microcarriers or adapting their method to produce hollow polymer-based microcarriers as now claimed.

The secondary references of Granet et al., Kusano et al., Henderson et al. and Starling et al. fail to remedy the deficiencies in the teachings of this primary reference as these references also fail to teach or suggest hollow polymer-based microcarriers or adaptation of their methods to produce such hollow polymer-based microcarriers.

Thus, the cited combination of prior art fails to teach or suggest all the limitations of the claims as amended and thus cannot render the instant claimed invention *prima facie* obvious.

Further, as taught at page 5 and demonstrated by experiments described at pages 10-13 of the instant application, scaffolds produced in accordance with the present invention circumvent limitations associated with static three-dimensional culturing methods such as taught by Devin et al., and increase the rate and extent of mineralized tissue formation in the rotating bioreactor as compared to prior art scaffolds. Such advantages are not obvious over the combined prior art teachings.

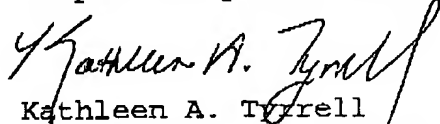
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Withdrawal of this rejection under 35 U.S.C. § 103(a) is therefore respectfully requested.

#### VI. Conclusion

Applicants believe that the foregoing comprises a full and complete response to the Office Action of record. Accordingly, favorable reconsideration and subsequent allowance of the pending claims is earnestly solicited.

Respectfully submitted,

  
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